

PETITION FOR EXTENSION OF TIME

Pursuant to 37 C.F.R. § 1.136(a), Applicants petition for an extension of time of third month to and including May 22, 2001 in which to respond to the Office Action dated November 22, 2000. Pursuant to 37 C.F.R. § 1.17, a check in the amount of \$445.00 is enclosed, which is/includes the process fee (\$445.00) for a three-month extension of time. If the check is inadvertently omitted, or should any additional fees under 37 C.F.R. §§ 1.16 to 1.21 be required for any reason relating to the enclosed materials, or should an overpayment be included herein, the Assistant Commissioner is authorized to deduct or credit said fees from or to Fulbright & Jaworski L.L.P. Deposit Account No. 50-1212/10024085/SLH. Please amend the application as follows.

AMENDMENTS

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In the Claims:

Please cancel claims 11-20 and amend the remaining claims as follows:

1. A method for producing disaggregated biologically active protein from a mixture comprising aggregated protein comprising the steps of:

- (a) adjusting total protein concentration in the mixture to from about 0.01 mg/mL to about 500 mg/mL; then
- (b) increasing the pressure on the mixture to from about 0.25 kbar to about 12 kbar for a time and temperature sufficient for disaggregation of the protein; then

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- (c) incubating the mixture under pressure in the range from about 0.25 kbar to about 3.3 kbar for a time from about 0.10 to about 12 hours; then
- (d) reducing the pressure to atmospheric pressure, whereby aggregated protein in the mixture is disaggregated and biological activity is retained.

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2. The method of claim 1, wherein during the incubations step (c), the mixture further comprises an oxidizing agent and a reducing agent wherein the oxidizing agent is oxidized glutathione and the reducing agent is dithiothreitol.
3. The method of claim 1, wherein the pressure in the incubation step (c), is from about 0.5 kbar to about 3.3 kbar.
4. The method of claim 3, further comprising adding, prior to step (b), a chaotropic agent at a concentration of from about 0.1 to about 8 M.
5. The method of claim 4, wherein during the incubation step (c), the protein concentration is from about 1 to about 100 mg/mL.
6. The method of claim 4, wherein during the incubation step (c), the protein concentration is from about 1 to about 20 mg/mL.
7. The method of claim 4, wherein after step (c), the concentration of the chaotropic agent is decreased to less than about 0.1 M.
- 10/8. The method of claim 1, wherein, prior to step (a), the aggregated protein is treated with a reducing agent.

- 12/10. The method of claim 9, wherein the detergent is selected from the group consisting of sodium dodecyl sulfate, polyethoxysorbitan, deoxycholate, sodium octyl sulfate, sodium tetradecyl sulfate, polyoxyethylene ethers, sodium cholate, octylthioglucopyranoside, n-octylglucopyranoside, alkyltrimethylammonium bromides, alkyltrimethyl ammonium chlorides, and sodium bis (2-ethylhexyl) sulfosuccinate.

Please add the following new claims:

- 8/21. The method of claim 4, wherein the chaotropic agent is guanidine hydrochloride.
- 9/22. The method of claim 21, wherein guanidine hydrochloride is present at a concentration of from about 0.1 to about 1 M.

REMARKS

I. Status of Claims

Claims 1-10 are pending and stand rejected under the first and second paragraphs of §112. The specific grounds for rejection, and applicants' responses thereto, are set out in detail below. Claims 1-8 and 10 are amended. New claims 21 and 22 are added.

II. Objection

The examiner objects to claim 10 on the grounds that an "and" is missing between the last two items of the Markush group. An appropriate amendment to claim 10 is offered.